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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,899	01/31/2007	Michal Eisenbach-Schwartz	EIS-SCHWARTZ32A	3343

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EXAMINER	
KIM, TAEYOON	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,899	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,26,28,29,31,32 and 34-37* is/are pending in the application.

4a) Of the above claim(s) *28 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,26,29,32 and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 4/8/2010 has been received and entered into the case.

Claims 1-23, 25, 27, 30 and 33 are canceled, claims 28 and 31 are withdrawn from consideration as being drawn to non-elected subject matter, and claims 24, 26, 29, 32 and 34-37 have been considered on the merits. All arguments have been fully considered.

It is noted that claim 29 was inadvertently missed out in the previous OA.

Considering the lack of enablement of the claimed invention, the claim rejection under 35 U.S.C.§102 is now withdrawn.

Claim Objections

Claim 36 is objected to because of the following informalities: the term "Copolymer" in line 7 would be "Copolymer 1." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 26, 29, 32 and 34-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating neuronal degeneration caused by glutamate toxicity or $A\beta_{1-40}$ toxicity in an animal model, does not reasonably provide enablement for treating or reducing progression a neurodegenerative disease such as Huntington's disease, or preventing neurodegeneration associated with HD. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or

use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The instant claims disclose a method of treating a neurodegenerative disorder or disease having accumulation of misfolded and/or aggregated proteins except prion-related diseases by administering Copolymer I to an individual suffering from the diseases or disorders; the claimed method are also for reducing progression, for protection from neurodegeneration, for protection from glutamate toxicity associated with HD.

The specification discloses examples and evidence showing that administration of Cop I reduced glutamate toxicity or $A\beta_{1-40}$ toxicity in retinal ganglion cells in an animal model (see Figures 1-9, 14 and Brief Description of the Figures at p.9-13). These descriptions are based on the animal model having been injected or immunized prior to glutamate toxicity or $A\beta_{1-40}$ toxicity.

However, the specification does not provide enabling embodiment showing that the administration or immunization of an individual suffering HD with Cop I and such treatment would be effective in HD patients.

While the specification discloses effective results from animal models, particularly R6/2

transgenic mice, for HD, this would not necessarily translate into human treatment. The specification of the instant application discloses a prophetic embodiment for human trial of HD treatment (Example 4 at p.31-32), and this would not be considered as evidence to support the efficacy of the claimed composition as an effective treatment to HD.

The state of the art is relatively low with regard to the treatment of HD. Despite extensive research activity in the art, the state of the art with regard to treating HD is broadly underdeveloped. In particular, there is no known agent that is effective in treating HD (emphasis added). According to the article on HD from National Institute of Neurological Disorders and Stroke, a number of medications available to help control emotional and movement problems associated with HD, but it is clear that there is no treatment to stop or reverse the course of the disease (p.6).

Furthermore, the website for Huntington's disease society of America (www.hdsa.org/about/our-mission/what-is-hd.html; downloaded on 6/2010) discloses that at present there is no effective treatment to halt the progression of HD or cure for HD (p.3-4).

The specification discloses that the etiology differs among neurodegenerative diseases, the propagation steps are similar, and cytotoxicity caused by excitatory amino acids, free radicals and nitric oxide is common to all the neurodegenerative disorders (p.4, lines 5-9), and glutamate is one of the most common mediators of toxicity (p.4, lines 10-16). However, the specification fails to disclose that the claimed method positively produce effective treatment in HD patients.

Applicant's limited disclosure based on animal model in glutamate toxicity is noted but is not sufficient to justify claiming a method of treatment for HD broadly.

The neurodegenerative diseases treatment art involves a very high level of

unpredictability. The lack of significant guidance from the present specification or prior art with regard to the actual treatment of HD in a human subject with the claimed active ingredient makes practicing the claimed invention unpredictable.

Absent a reasonable *a priori* expectation of success for using a specific agent or combination of agents to treat these neurodegenerative diseases, one skilled in the art would have to extensively test many various patients in many various stages of the disease. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as it is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Response to Arguments

Applicant's arguments have been fully considered but they are not persuasive. In the response to the enablement rejection, applicant alleged that the specification provides sufficient to enable the claimed treatment of a neurodegenerative disorder or disease in which there is accumulation of misfolded and/or aggregated proteins, such as HD. Applicant further alleged that HD R6/2 transgenic mice over-expressing exon 1 of the human HD gene and have been used widely as a recognized or accepted animal model of human HD.

While it is acknowledged that HD R6/2 transgenic mice is a well known animal model for HD, however, this animal model is not the same as human HD, and considering the unknown etiology of HD, and the HD gene, huntingtin, is one identified characteristics of HD, the animal model cannot be considered the same as human HD. Therefore, it is not predictable whether the treatment to the animal model would necessarily work and produce the same results in real HD

without undue experimentation.

As applicant also discussed, enablement is considered in view of the Wands factors (MPEP 2164.01 (a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " *(Wands,* 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *(Wands,* 8 USPQ2d 1404).

The results obtained from animal models would not necessarily translate into human treatment. The animal model of HD, R6/2 transgenic mice, has been developed by Mangiarini et al. in 1996. Ever since the introduction of this animal model, numerous studies and research for a potential treatment were carried out. However, so far there is no known effective treatment for human HD.

The specification of the instant application discloses a prophetic embodiment for human trial of HD treatment (Example 4 at p.31-32), and this would not be considered as evidence to support the efficacy of the claimed composition as an effective treatment to HD.

In order to obtain validity for human treatment of the efficacy resulted from animal models, clinical trial is a next step. Clinical trial is not a routine experimentation, and requires extensive and undue experimentations. Furthermore, as discussed above, none of potential drugs

identified from animal models including R6/2 transgenic mice did not produce effective treatment to human disease.

Bates et al. (2003, Current Opinion in Neurology) discussed that animal models including R6/2 transgenic mice would be useful tools to identify a potential therapeutic compounds but these will only be validated once they have delivered a therapy that shows efficacy in the clinic (p.469, left col.). The disclosure of the instant specification shows that the compounds claimed are effective in animal models of HD, but this result would not necessarily translate into efficacy of HD in the clinic. Bates et al. further suggest that the first successful treatments for Huntingdon's disease might be composed of combinations of drugs each of which makes a small contribution to the overall beneficial effect (p.469, right col.). Therefore, it is hardly predictable that the results disclosed in the current application based on the animal model would effectively produce the same results in treating HD without undue experimentations.

Thus, the specification of the instant application is not considered to enable a person of ordinary skill in the art to use the method to treat HD without undue experimentation.

Claim 29 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claim discloses a new limitation of "therapeutically effective amount." However, the specification does not provide any detail that the inventor had possession of the claimed invention. There is no disclosure of any amount of claimed compound for the effective

outcome of reducing disease progression, protection from neurodegeneration, or glutamate toxicity in HD patients.

M.P.E.P. §2163 states "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116."

M.P.E.P. § 2163 also recites, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention… one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." and further, "The description needed to satisfy the requirements of 35 U.S.C. 112 "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d at 1357, 76 USPQ2d at 1084.< Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. In most technologies which are mature, and wherein the knowledge and level of skill in the art is high, a written description question should not be raised for claims >present in the application when originally filed,< even if the specification discloses only a method of making the invention and the function of the invention. See, e.g., *In re Hayes Microcomputer Products, Inc. Patent Litigation*, 982 F.2d 1527,

1534-35, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992) ("One skilled in the art would know how to program a microprocessor to perform the necessary steps described in the specification. Thus, an inventor is not required to describe every detail of his invention. An applicant's disclosure obligation varies according to the art to which the invention pertains. Disclosing a microprocessor capable of performing certain functions is sufficient to satisfy the requirement of section 112, first paragraph, when one skilled in the relevant art would understand what is intended and know how to carry it out."). In contrast, for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession."

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651